Stereocontrolled IMDA Reaction of Styrene Derivatives. A Way to Enantiopure 3a,4,9,9a-Tetrahydrobenz[*f*]isoindolines

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IMDA reactions on chiral perhydro-1,3-benzoxazines, derived from (−)-8-amino menthol, bearing a styrene substituent at C-2 acting as diene and an acryl amide acting as dienophile occur with high stereoselection and excellent chemical yields. After elimination of the chiral appendage, enantiopure 3a,4,9,9a-tetrahydrobenz[*f*]isoindolines are prepared in this way. The effect of the substituents at both diene and dienophile are studied, showing that a methyl group at C-1 in the diene inhibited the reaction, while the ene adduct, instead of the IMDA product, was obtained when a methyl group was at C-2.

Introduction

The intramolecular Diels−Alder reaction (IMDA) constitutes one of the most employed methods in the construction of polycyclic systems because in addition to the general features of the intermolecular version it enjoys improved regio- and stereochemical control.[1] The synthesis of benzo derivatives by using styrenes as dienes in both inter- and intramolecular Diels−Alder reactions has been well-known for more than 25 years,[2] although styrenes are usually poor dienes because the initial step entails loss of aromatic resonance stabilization and harsh reaction conditions are needed for the intermolecular processes. However, quite mild reaction conditions are required for IMDA reactions, and styrene effectively participates as the diene in the formation of benzannulated systems after rearomatization by a 1,3-hydrogen shift in the intermediate.[3]

Recently, interest in the use of styrenes or their aza analogues[4] came up again in the synthesis of carbo- and heterocycles in both inter-[5] or intramolecular[6] Diels−Alder reactions, but there are only a few antecedents on the diastereoselective IMDA reaction using styrenes as dienes.[7]

In connection with a project directed toward the exploitation of the IMDA reaction in the stereoselective synthesis of heterocyclic systems[8] we report now on the synthesis of enantiopure 3a,4,9,9a-tetrahydrobenz[*f*]-isoindolines **10** by using a styrene derivative as the diene and an α,*β*-unsaturated amide as the dienophile attached to a chiral perhydro-1,3-benzoxazine derived from (−)-8-aminomenthol acting as chiral template (Figure 1). These isoindoline derivatives are of biological interest because some of them have analgesic,[9] antidepressant,[10] antihypertensive,[11] or antiasthmatic or antiallergic[12] activities.

Results and Discussion

Chiral 2-styryl-3-acryloyl and methacryloyl perhydro-1,3-benzoxazines **2a**−**h** were prepared in two steps by acylation of 2-styryl perhydro-1,3-benzoxazines, which in turn were obtained by condensation of (−)-8-aminomenthol[13] with cinnamaldehyde derivatives in toluene at reflux (Scheme 1). All α,*β*-unsaturated aldehydes were commercially available except *trans*-*β*-methylcinnamaldehyde, which was prepared by lithium aluminum hydride reduction of ethyl *trans*-*β*-methylcinnamate to the alcohol, followed by Swern oxidation to the aldehyde in 83% total yield.[14]

The acylation was carried out with acryloyl or methacryloyl chloride at 0 °C in the presence of triethylamine or TMEDA respectively, using methylene chloride as solvent. The chromatographic purification of the compounds must be done on silica gel deactivated with triethylamine; otherwise, the products were partially hy-

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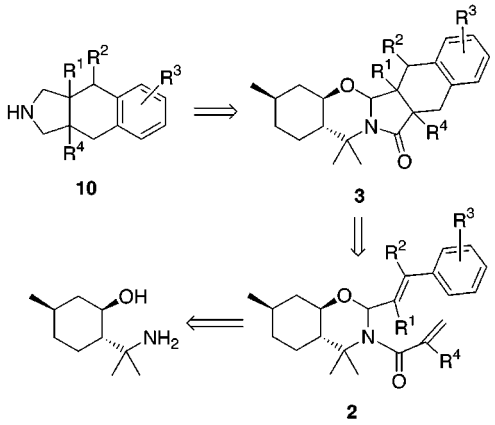
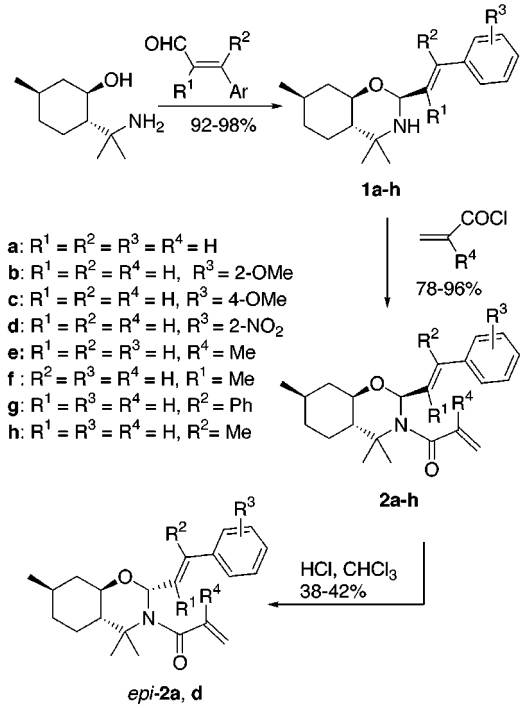


Figure 1. Retrosynthetic analysis of tetrahydrobenz[*f*]isoindolines.

Scheme 1



drolyzed to 8-(*N*-acryloyl)amino menthol or were epimerized at C-2. The epimerization could also be promoted by acidic treatment. In this way, **2a** and **2d** were transformed into *epi*-**2a** and *epi*-**2d** in moderate yield by stirring, at room temperature, with a solution of anhydrous HCl in chloroform.

Thermal cyclization reactions were carried out under different experimental conditions, and the results are summarized in Scheme 2 and Table 1. Thermolysis of the parent compound **2a** was tested under different reaction conditions (entries 1−4 in Table 1), observing that the reaction was not complete after refluxing in THF, hexane or acetonitrile for 48 h or by heating in toluene at 60 °C for 20 h, and starting amide was recovered in different amounts. On the contrary, **2a** gave a very clean conversion, with excellent yield, of two (of the possible four) cycloadducts by refluxing for 3 h in toluene or DMF (entries 5 and 6 in Table 1). Interestingly, under these reaction conditions, improvements not only in chemical yields but also in the diastereomeric ratios were observed, although only negligible effects

Scheme 2

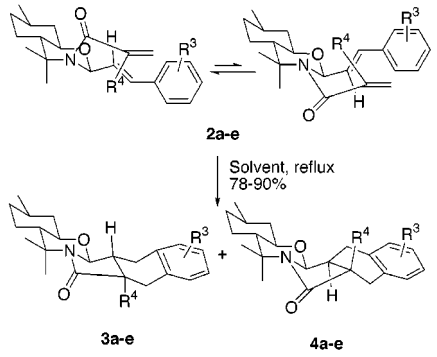


Table 1. Diels−Alder Reaction of Amides 2a−h, *epi*-2a, and *epi*-2d

entry	amide	solvent	time (h)	*T* (°C)	yield[a] (%)	product ratio[b] (%)
1	**2a**	THF	48	66	55[c]	**3a** (72), **4a** (28)
2	**2a**	hexane	48	69	22[d]	**3a** (75), **4a** (25)
3	**2a**	CH_3CN	48	82	65[e]	**3a** (79), **4a** (21)
4	**2a**	toluene	20	60	55[f]	**3a** (78), **4a** (22)
5	**2a**	toluene	3	110	88	**3a** (80), **4a** (20)
6	**2a**	DMF	3	153	81	**3a** (86), **4a** (14)
7	**2b**	toluene	3.5	110	86	**3b** (86), **4a** (14)
8	**2b**	DMF	3.5	153	82	**3b** (81), **4b** (19)
9	**2c**	toluene	3.5	110	81	**3c** (89), **4c** (11)
10	**2c**	DMF	3.5	153	78	**3c** (96), **4c** (4)
11	**2d**	toluene	3.5	110	85	**3d** (85), **4d** (15)
12	**2d**	DMF	3.5	153	90	**3d** (83), **4d** (17)
13	**2e**	toluene	4.5	110	75	**3e** (75), **4e** (25)
14	**2e**	DMF	4	153	84	**3e** (90), **4e** (10)
15	**2f**	toluene	22	110	5[g]	
16	**2g**	toluene	3.5	110	86	**3g** (82), **5** (18)
17	**2g**	DMF	3.5	153	83	**3g** (90), **5** (10)
18	**2h**	toluene	3	110	90	**6** (100)
19	*epi*-**2a**	toluene	3.5	110	79	*epi*-**3a** (87), *epi*-**4a** (13)
20	*epi*-**2d**	toluene	3.5	110	89	*epi*-**3d** (89), *epi*-**4d** (11)

[a] Chemical yields of pure, isolated compounds. [b] Determined by integration of the signals in ^{1}H NMR spectra of the reaction mixtures. [c] 32%. [d] 60%. [e] 8%. [f] 12% of amide **2a** was recovered. [g] 85% of amide **2e** was recovered.

were observed in both the yield and the facial discrimination when toluene was changed to DMF as solvent.

The presence of an electron-withdrawing nitro group in the aromatic styrene ring (entries 11, 12, and 20 in Table 1) provided an example of an IMDA reaction between two electron-deficient counterparts with excellent chemical yields and good stereoselection. A similar behavior was observed for dienes **2b** and **2c** with an electron-donor methoxy substituent on the phenyl group (entries 7−10 in Table 1). In this case, only traces of the minor cycloadduct **4c** were obtained when the cyclization was carried out in DMF (entry 10 in Table 1). It is worth noting that these reactions showed total exo/endo selectivity, and endo adducts were not detected in the reaction mixtures. These results contrast with those previously reported for reactions with open dienes, where minor endo cycloadducts are always formed.[8b,15]

The relative stereochemistry of the stereocenters where diene and dienophile are attached was studied on epimerized perhydro-1,3-benzoxazines *epi*-**2a** and *epi*-**2d**. The cyclization of these substrates in refluxing toluene also

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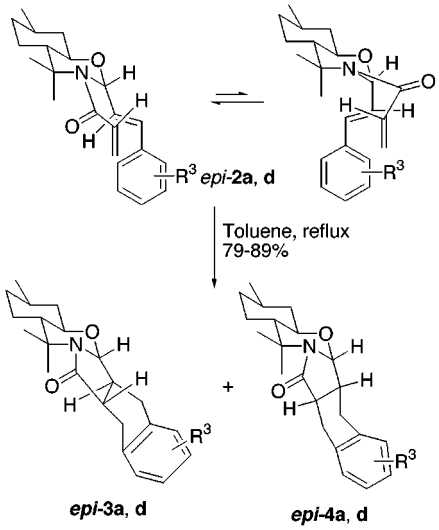
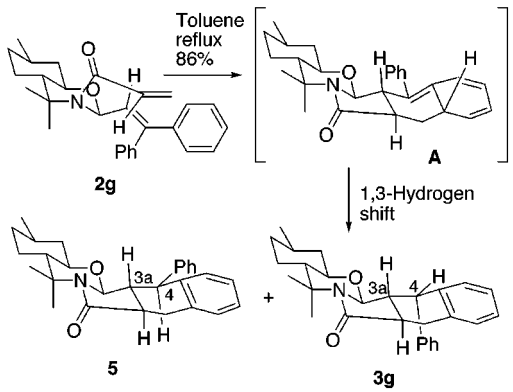
Scheme 3



Scheme 4

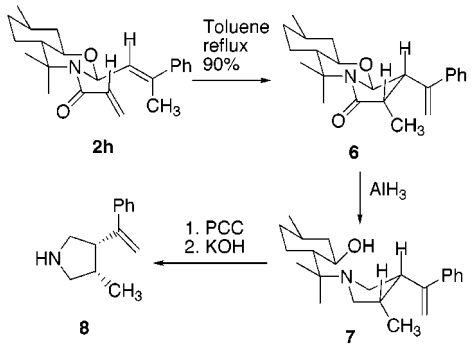


gave exo adducts *epi*-**3a**,**d** and *epi*-**4a**,**d** in good chemical yields and de (entries 19 and 20 in Table 1 and Scheme 3).

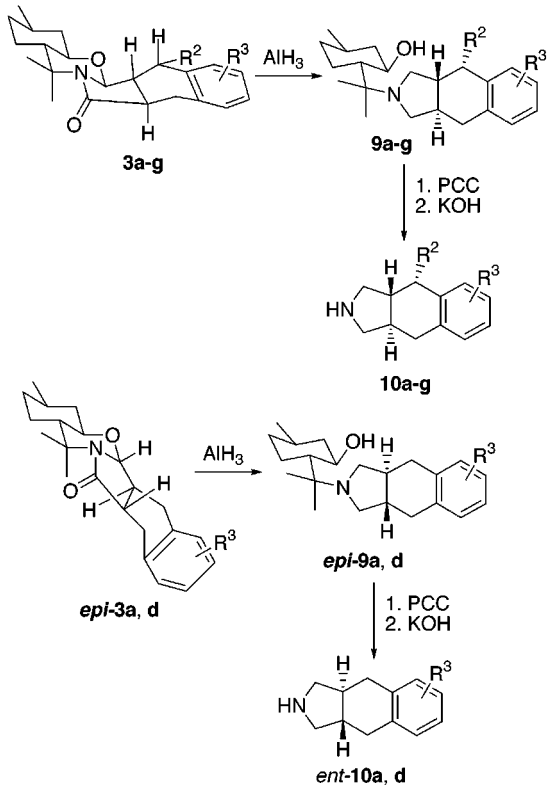
The influence of substituents at both styrene and dienophile was tested in compounds **2e** and **2h**. Perhydro-1,3-benzoxazine **2e**, with a methyl group at the inner carbon of the dienophile, easily cyclized to the corresponding adducts, although the facial discrimination decreased to 3:1 when the reaction was carried out in toluene at reflux (entry 13 in Table 1). Surprisingly, compound **2f**, with a methyl group at C-1 in the diene component, was inefficient in the IMDA reaction, giving rise to a mixture of cyclization products, in only 5% yield after refluxing in toluene for 22h (entry 15 in Table 1). On the contrary, compound **2g**, with a phenyl group at C-2 in the diene easily cyclized to exo adduct **3g** along with 10% of diastereomer **5** (entry 17 and Scheme 4). The stereochemical relationship of the substituents at C-3a and C-4 (benzoisoindoline numbering) in compounds **3g** and **5** shows that both are formed by rearomatization of a single common exo cyclization intermediate **A** (Scheme 4). The migration of the hydrogen occurs by a formally suprafacial 1,3-hydrogen shift, giving component **3g** or in a formally antarafacial fashion leading to the minor isomer **5**.

Thermolysis of the compound **2h** with a methyl substituent at C-2 in the diene gave a rapid reaction and was totally stereoselective, providing the ene adduct **6** as a single compound in 90% yield, instead the IMDA reaction product (Scheme 5)

Scheme 5



Scheme 6



All diastereomers formed in the reactions were isolated and purified by flash chromatography and obtained as crystalline solids (except minor adducts **4c** and *epi*-**4a** that were not obtained pure), and the stereochemistry was determined at this stage. COSY and NOESY experiments allowed the establishment of the stereochemistry for **3b**−**d**, *epi*-**3d**, and **4b**,**d**, whereas the configuration for **3a**,**g**, **5**, and *epi*-**3a** was determined by X-ray diffraction studies.

Adducts **3a**−**e**,**g** were converted into enantiopure 3a,4,9,9a-tetrahydrobenz[*f*]isoindolines **10a**−**e**,**g** and *epi*-**3a**,**d** and **4a** into *ent*-**10a**,**d**, respectively, as depicted in Scheme 6. In this way, treatment of the adducts with aluminum hydride in THF at −10 °C furnished aminomenthol derivatives **9a**−**g** or *epi*-**9a**,**d** in very good chemical yields (80−94%), which upon oxidation with PCC in methylene chloride at rt, followed by treatment with a 2.5 M solution of KOH in THF−MeOH, yielded the final enantiopure isoindoline derivatives in good yields (62−82%). The same treatment on adduct **6** led to the enantiopure pyrrolidine **8** in 82% yield (Scheme 5).

In summary, the described IMDA reaction using styrene derivatives as the diene provides a novel and stereoselective synthesis of enantiopure 3a,4,9,9a-tetrahydrobenz[*f*]isoindolines. Both enantiomers can be obtained simply by starting from epimeric perhydro-1,3-benzoxazines.

Experimental Section

General Methods. All reactions were carried out in anhydrous solvents, under argon atmosphere and in oven-dried glassware. TLC was performed on glass-backed plates coated with silica gel 60 with an F 254 indicator. Products were isolated by flash chromatography using 240−400 mesh silica gel. Melting points were determined in capillary tubes and are uncorrected. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were registered in $CDCl_3$ or DMSO-d_6 as solvent and TMS as internal standard. Chemical shifts are given in ppm. Optical rotations were determined on a digital polarimeter using a sodium lamp, and concentration is given in g per 100 mL. Mass spectra were recorded by electronic impact or chemical ionization.

Synthesis of Perhydrobenzoxazines 1a−g. A mixture of 8-(−)-aminomenthol (5 g, 29.24 mmol) and the appropriate cinnamaldehyde derivative (30 mmol) in toluene (50 mL) was refluxed until the reaction was completed (TLC, 3−5 h). The solvent was evaporated under vacuum and the residue was purified by recrystallization or by flash chomatography on silica gel deactivated with triethylamine with hexane/EtOAc 8/1 as eluent. Perhydrobenzoxazines **1a**,**b**,**f**,**g** have been previously described.[16]

2α-[2-*trans*-(4′-Methoxyphenyl)ethenyl]-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (1c). Yield: 92%. Colorless oil. $[\alpha]^{25}_D = +28.0$ ($c = 1.1$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.09−1.21 (m, 4H); 0.93 (d, 3H, $J = 6.6$ Hz); 1.11 (s, 3H); 1.14 (s, 3H); 1.38−1.55 (m, 1H); 1.63−1.70 (m, 3H); 1.98 (m, 1H); 3.50 (dt, 1H, $J_1 = 4.2$ Hz, $J_2 = 10.5$ Hz); 3.76 (s, 3H); 4.96 (dd, 1H, $J_1 = 1.1$ Hz, $J_2 = 4.8$ Hz); 6.04 (dd, 1H, $J_1 = 4.8$ Hz, $J_2 = 16.0$ Hz); 6.68 (dd, 1H, $J_2 = 1.1$ Hz, $J_2 = 16.0$ Hz); 6.81 (d, 2H, $J = 8.8$ Hz); 7.31 (d, 2H, $J = 8.8$ Hz). ^{13}C NMR ($CDCl_3$) δ: 19.5; 22.2; 25.4; 29.7; 31.2; 34.8; 41.5; 51.2; 51.4; 55.0; 74.8; 82.1; 113.6 (2C); 125.8; 127.7 (2C); 129.1; 130.9; 159.1. IR (film): 3050; 2900; 1570; 800; 750 cm^{-1}. MS (*m*/*z*): 315 (M^+, 10); 160 (76); 134 (58); 55 (46); 41 (100).

2α-[2-*trans*-(2′-Nitrophenyl)ethenyl]-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (1d). Yield: 94%. Colorless oil. $[\alpha]^{25}_D = +2.5$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.91−1.11 (m, 4H); 1.12 (d, 3H, $J = 6.2$ Hz); 1.13 (s, 3H); 1.15 (s, 3H); 1.47−1.58 (m, 2H); 1.65−1.74 (m, 2H); 1.98 (m, 1H); 3.53 (dt, 1H, $J_1 = 4.1$ Hz, $J_2 = 10.4$ Hz); 5.03 (dd, 1H $J_1 = 1.0$ Hz $J_2 = 4.4$ Hz); 6.18 (dd, 1H $J_1 = 4.4$ Hz $J_2 = 15.8$ Hz); 7.25 (dd, 1H, $J_1 = 1.0$ Hz, $J_2 = 15.8$ Hz); 7.35−7.41 (m, 1H); 7.51−7.62 (m, 2H); 7.90 (dd, 1H, $J_1 = 1.2$ Hz, $J_2 = 8.2$ Hz). ^{13}C NMR ($CDCl_3$) δ: 19.5; 22.4; 25.8; 30.0; 31.6: 35.1; 41.9; 51.8 (2C); 75.2; 81.7; 124.5; 127.0; 128.2; 128.4; 132.3; 133.1; 133.8; 148.1. IR (film): 3050; 2900; 1605; 1580; 780; 745 cm^{-1}. MS (*m*/*z*): 332 ($M^+ + 2$, 25); 331 ($M^+ + 1$, 100); 329 ($M^+ - 1$, 7).

2α-(*trans*-2-Methyl-2-phenylethenyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (1h). Yield: 92%. Colorless oil. $[\alpha]^{25}_D = +12.5$ ($c = 1.1$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.90−1.09 (m, 4H); 0.92 (d, 3H, $J = 6.5$ Hz); 1.10 (s, 3H); 1.17 (s, 3H); 1.46−1.70 (m, 4H); 1.93−2.00 (m, 1H); 2.14 (d, 3H, $J = 1.2$ Hz); 3.52 (dt, 1H, $J_1 = 4.2$ Hz, $J_2 = 10.4$ Hz); 5.18 (d, 1H, $J = 6.8$ Hz); 5.68 (dd, 1H, $J_1 = 1.2$ Hz, $J_2 = 6.8$ Hz); 7.17−7.29 (m, 3H); 7.38−7.42 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 16.5; 19.4; 22.1; 25.4; 29.7; 31.2; 34.8; 41.5; 51.1; 51.2; 74.7; 79.9; 125.7 (2C); 126.1; 127.0; 127.8 (2C); 138.9; 142.4. IR (film): 3050; 2910; 755; 695 cm^{-1}. MS (*m*/*z*): 301 ($M^+ + 2$, 21); 300 ($M^+ + 1$, 100); 182 (26).

Synthesis of Amides 2a−h. To a mixture of the appropiate perhydrobenzoxazine (17.5 mmol) and triethylamine (3.05 mL, 21.9 mmol) in anhydrous CH_2Cl_2 (50 mL) at 0 °C was slowly added a solution of acryloyl chloride (1.63 mL, 20.1 mmol) in CH_2Cl_2 (25 mL). The stirring was continued until the reaction was finished (TLC, 2−3 h), and then a saturated aqueous solution of $NaHCO_3$ (50 mL) was added and the resulting mixture stirred at room temperature for additional 2 h. The aqueous phase was extracted twice with CH_2Cl_2, and the organic layer was washed with water and dried over anhydrous $MgSO_4$. The solvent was evaporated, and the residue was purified by flash chromatography on deactivated silica gel with hexane/EtOAc 10/1 as eluent. Preparation of amide **2h** was carried out by a similar way by slow addition of a solution of methacryloyl chloride (2.0 mL, 20.1 mmol) in CH_2Cl_2 to a mixture of perhydrobenzoxazine **1a** (5 g, 17.5 mmol) and TMDA (3.3 mL, 21.9 mmol) in CH_2Cl_2 (50 mL).

***N*-Acryloyl-2α-(2-*trans*-phenylethenyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (2a).** Yield: 90%. Colorless solid. Mp: 86−87 °C (from hexane). $[\alpha]^{25}_D = -32.5$ ($c = 1.1$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.85 (m, 1H); 0.93 (d, 3H, $J = 6.5$ Hz); 1.03−1.19 (m, 2H); 1.47 (m, 1H); 1.56 (s, 3H); 1.63−1.78 (m, 2H); 1.68 (s, 3H); 2.03−2.12 (m, 2H); 3.72 (dt, 1H, $J_1 = 3.9$ Hz, $J_2 = 11.4$ Hz); 5.59 (dd, 1H, $J_1 = 2.2$ Hz, $J_2 = 10.2$ Hz); 5.91 (dd, 1H, $J_1 = 1.9$ Hz; $J_2 = 2.2$ Hz); 6.24 (dd, 1H, $J_1 = 2.2$ Hz, $J_2 = 16.8$ Hz); 6.38 (dd, 1H, $J_1 = 10.2$ Hz, $J_2 = 16.8$ Hz); 6.46 (dd, 1H, $J_1 = 2.4$ Hz, $J_2 = 16.2$ Hz); 6.57 (dd, 1H, $J_1 = 1.9$ Hz, $J_2 = 16.2$ Hz); 7.27−7.42 (m, 5H). ^{13}C NMR ($CDCl_3$) δ:18.9; 21.9; 24.5; 25.2; 31.5; 34.3; 43.7; 46.1; 58.0; 73.5; 81.9; 126.7(2C); 127.2; 128.2; 128.7(2C); 130.8; 131.5; 132.0; 135.8; 166.5. IR (Nujol): 3020; 1640; 1610; 750; 780; 770; 690 cm^{-1}. MS (*m*/*z*): 340 ($M^+ + 1$, 100); 263 (24); 208 (46); 186 (64). Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 77.62; H, 8.79; N, 4.30.

***N*-Acryloyl-2α-[2-*trans*-(2′-methoxyphenyl)ethenyl]-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (2b).** Yield: 92%. Colorless solid. Mp: 68−69 °C (from hexane/EtOAc 10/1). $[\alpha]^{25}_D = -46.6$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.71−1.21 (m, 3H); 0.93 (d, 3H, $J = 6.5$ Hz); 1.30−1.50 (m, 1H); 1.56 (s, 3H); 1.68 (s, 3H); 1.69−1.79 (m, 2H); 2.06−2.20 (m, 2H); 3.71 (dt, 1H, $J_1 = 3.9$ Hz, $J_2 = 11.3$ Hz); 3.83 (s, 3H); 5.57 (dd, 1H, $J_1 = 1.8$ Hz, $J_2 = 10.4$ Hz); 5.89 (dd, 1H, $J_1 = 1.8$ Hz, $J_2 = 2.5$ Hz); 6.21 (dd, 1H, $J_1 = 1.8$ Hz, $J_1 = 16.8$ Hz); 6.39 (dd, 1H, $J_1 = 10.4$ Hz, $J_1 = 16.8$ Hz); 6.46 (dd, 1H, $J_1 = 2.5$ Hz, $J_1 = 16.4$ Hz); 6.88−6.99 (m, 3H); 7.27 (dd, 1H, $J_1 = 6.9$ Hz, $J_1 = 8.6$ Hz); 7.40 (d, 1H, $J = 7.5$ Hz). ^{13}C NMR ($CDCl_3$) δ: 18.8; 21.8; 24.2; 25.2; 31.5; 34.3; 43.6; 45.8; 55.3; 58.0; 73.6; 82.3; 110.8; 120.5; 125.0; 126.7 (2C); 127.1; 129.1; 131.0; 132.4; 156.9; 166.7. IR (Nujol): 3050; 1640; 1600; 750 cm^{-1}. MS (*m*/*z*): 370 ($M^+ + 1$, 15); 208 (43); 177 (100). Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.57; H, 8.32; N, 3.96.

***N*-Acryloyl-2α-[2-*trans*-(4′-methoxyphenyl)ethenyl]-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (2c).** Yield: 92%. Colorless oil. $[\alpha]^{25}_D = -46.9$ ($c = 1.4$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.54 (m, 4H); 0.92 (d, 3H, $J = 6.6$ Hz); 1.56 (s, 3H); 1.67 (s, 3H); 1.71−1.77 (m, 2H); 2.06−2.15 (m, 2H); 3.70 (dt, 1H, $J_1 = 3.9$ Hz, $J_2 = 11.5$ Hz); 3.81 (s, 3H); 5.58 (dd, 1H, $J_1 = 2.2$ Hz, $J_2 = 10.2$ Hz); 5.89 (dd, 1H, $J_1 = 2.0$, $J_2 = 2.6$ Hz); 6.23 (dd, 1H, $J_1 = 2.2$ Hz, $J_2 = 16.7$ Hz); 6.31 (dd, 1H, $J_1 = 2.6$ Hz, $J_2 = 16.2$ Hz); 6.38 (dd, 1H, $J_1 = 10.2$ Hz, $J_2 = 16.7$ Hz); 6.51 (dd, 1H, $J_1 = 2.0$ Hz, $J_2 = 16.2$ Hz); 6.90 (d, 2H, $J = 8.8$ Hz); 7.33 (d, 2H, $J = 8.8$ Hz). ^{13}C NMR ($CDCl_3$) δ: 18.7; 21.7; 24.3; 25.1; 31.4; 34.2; 43.6; 45.9; 55.1; 57.8; 73.4; 81.9; 114 (2C); 126.9; 127.7 (2C); 128.4; 129.5; 130.7; 130.8; 159.5; 166.4. IR (film): 3050; 1660; 1600; 730 cm^{-1}. MS (*m*/*z*): 369 (M^+, 10); 159 (33); 95 (48); 81 (94); 55 (100). Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.89; H, 8.27; N, 3.61.

***N*-Acryloyl-2α-[2-*trans*-(2′-nitrophenyl)ethenyl]-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (2d).** Yield: 94%. Colorless solid. Mp: 134−135 °C (from hexanes−EtOAc 8:1). $[\alpha]^{25}_D = -13.7$ ($c = 1.2$, $CHCl_3$). ^{1}H ($CDCl_3$) δ: 0.89−0.99 (m, 1H); 0.94 (d, 3H, $J = 6.5$ Hz); 0.98−1.50 (m, 3H); 1.57 (s, 3H); 1.69 (s, 3H); 1.67−1.79 (m, 1H); 1.80−1.85 (m, 1H); 2.08 (m, 1H); 2.19 (dt, 1H, $J_1 = 3.1$ Hz, $J_2 = 11.5$ Hz); 3.75 (td, 1H, $J_1 = 4.0$ Hz, $J_2 = 11.5$ Hz); 5.63 (dd, 1H, $J_1 = 2.1$ Hz, $J_2 =$

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10.3 Hz); 5.94 (dd, 1H, $J_1 = 2.2$, $J_2 = 2.5$ Hz); 6.24 (dd, 1H, $J_1 = 2.1$ Hz, $J_2 = 16.7$ Hz); 6.38 (dd, 1H, $J_1 = 2.5$ Hz, $J_2 = 15.9$); 6.41 (dd, 1H, $J_1 = 10.3$ Hz, $J_2 = 16.7$ Hz); 7.05 (dd, 1H, $J_1 = 2.2$ Hz, $J_2 = 15.9$ Hz); 7.47 (ddd, 1H, $J_1 = 1.5$ Hz, $J_2 = 7.8$ Hz, $J_3 = 8.2$ Hz); 7.54 (dd, 1H, $J_1 = 1.5$ Hz, $J_2 = 7.8$ Hz); 7.64 (dt, 1H, $J_1 = 1.1$ Hz, $J_2 = 7.8$ Hz); 8.01 (dd, 1H, $J_1 = 1.0$ Hz, $J_2 = 8.2$ Hz). ^{13}C NMR ($CDCl_3$) δ: 19.0; 21.8; 24.4; 25.2; 31.5; 34.3; 43.4; 45.9; 58.0; 73.7; 81.6; 124.7; 127.3; 127.6; 128.6; 129.1; 130.7; 132.2; 133.4; 137.1; 147.6; 166.6. IR (Nujol): 3050; 1640; 1605; 780; 760; 730; 680. cm^{-1}. MS (*m*/*z*): ($M^+ + 1$, 46); 209 (14); 208 (100); 192 (55). Anal. Calcd for $C_{22}H_{28}N_2O_4$: C, 68.73; H, 7.34; N, 7.29. Found: C, 68.52; H, 7.16; N, 7.38.

***N*-Methacryloyl-2α-(2-*trans*-phenylethenyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (2e).** Yield: 96%. Colorless oil. $[\alpha]^{25}_D = -4.1$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.81−1.22 (m, 3H); 0.93 (d, 3H, $J = 6.5$ Hz); 1.44−1.49 (m, 1H); 1.52 (s, 3H); 1.68 (s, 3H); 1.64−1.75 (m, 2H); 1.96 (s, 3H); 2.09−2.17 (m, 2H); 3.73 (dt, 1H, $J_1 = 4.1$ Hz, $J_2 = 11.3$ Hz); 5.04−5.07 (m, 2H); 5.94 (m, 1H); 6.39 (dd, 1H, $J_1 = 3.0$ Hz, $J_2 = 16.2$ Hz); 6.60 (dd, 1H, $J_1 = 1.7$ Hz, $J_2 = 16.2$ Hz); 7.27−7.40 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 18.1; 20.3; 21.7; 24.8; 25.1; 31.2; 34.1; 43.5; 46.0; 57.9; 72.9; 82.1; 114.2; 126.3 (2C); 127.9; 128.5 (2C); 130.9; 132.4; 135.8; 142.2; 172.3. IR (film): 3070; 3020; 1630; 750; 720; 685. cm^{-1}. Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 78.34; H, 8.69; N, 4.14.

***N*-Acryloyl-2α-(*trans*-1-methyl-2-phenylethenyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (2f).** Yield: 85%. Colorless oil. $[\alpha]^{25}_D = -3.3$ ($c = 1.1$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.83−1.39 (m, 3H); 0.93 (d, 3H, $J = 6.5$ Hz); 1.45−1.56 (m, 1H); 1.58 (s, 3H); 1.71 (s, 3H); 1.67−1.77 (m, 2H); 1.99 (d, 3H, $J = 1.0$ Hz); 2.05−2.13 (m, 2H); 3.73 (dt, 1H, $J_1 = 3.8$ Hz, $J_2 = 11.6$ Hz); 5.56−5.61 (m, 2H); 6.25−6.27 (m, 2H); 6.70 (d, 1H, $J = 1.0$ Hz); 7.24−7.36 (m, 3H); 7.37−7.41 (m, 2H). ^{13}C NMR ($CDCl_3$) (δ): 15.8; 19.1; 21.9; 24.0; 25.2; 31.7; 34.5; 43.2; 45.7; 58.0; 74.2; 86.4; 127.0; 127.2; 127.6; 128.3 (2C); 128.9 (2C); 131.1; 136.9; 139.7; 167.2. IR (film): 3040; 3005; 1640; 1600; 790; 740; 695. cm^{-1}. MS (*m*/*z*): 354 ($M^+ + 1$, 39); 236 (31); 208 (100); 200 (87). Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 77.92; H, 9.03; N, 3.78.

***N*-Acryloyl-2α-(2,2-diphenylethenyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (2g).** Yield: 88%. Colorless solid. Mp: 122−123 °C (from hexanes−EtOAc 10:1). $[\alpha]^{25}_D = -188.0$ ($c = 1.1$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.90−1.11 (m, 1H); 0.93 (d, 3H, $J = 6.5$ Hz); 1.13−1.25 (m, 2H); 1.45−1.50 (m, 1H); 1.48 (s, 3H); 1.73 (s, 3H); 1.70−1.75 (m, 1H); 1.85 (m, 1H); 2.01−2.09 (m, 2H); 3.69 (dt, 1H, $J_1 = 3.8$ Hz, $J_2 = 11.3$ Hz); 5.24 (dd, 1H, $J_1 = 2.3$ Hz, $J_2 = 10.1$ Hz); 5.51 (d, 1H, $J = 8.6$ Hz); 5.85 (dd, 1H, $J_1 = 10.1$ Hz, $J_2 = 16.8$ Hz); 5.96 (dd, 1H, $J_1 = 2.3$ Hz, $J_2 = 16.8$ Hz); 6.29 (d, 1H, $J = 8.6$ Hz); 7.23−7.41 (m, 10H). ^{13}C NMR ($CDCl_3$) δ: 18.6; 21.7; 25.1; 25.4; 31.5; 34.4; 43.4; 47.7; 57.9; 73.0; 80.2; 125.9; 127.8 (2C); 128.0 (3C); 128.2 (3C); 128.9; 129.7 (2C); 130.6; 137.8; 141.4; 145.2; 166.7. IR (Nujol): 3010; 1680; 1620; 760; 750; 720; 700; 690. cm^{-1}. MS (*m*/*z*): 416 ($M^+ + 1$, 62); 262 (52); 236 (35); 223 (62), 208 (100). Anal. Calcd for $C_{28}H_{33}NO_2$: C, 80.93; H, 8.00; N, 3.37. Found: C, 81.12; H, 7.89; N, 3.52.

***N*-Acryloyl-2α-(*trans*-2-methyl-2-phenylethenyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (2h).** Yield: 78%. Colorless oil. $[\alpha]^{25}_D = -6.1$ ($c = 1.3$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.79−1.28 (m, 3H); 0.87 (d, 3H, $J = 6.5$ Hz); 1.35−1.53 (m, 1H); 1.55 (s, 3H); 1.66−1.81 (m, 2H); 1.68 (s, 3H); 1.98−2.04 (m, 2H); 2.16 (s, 3H); 3.67 (dt, 1H, $J_1 = 3.6$ Hz, $J_2 = 11.5$ Hz); 5.55 (dd, 1H, $J_1 =$2.1 Hz, $J_2 = 10.3$ Hz); 5.95−5.98 (m, 2H); 6.16 (dd, 1H, $J_1 = 2.1$ Hz, $J_2 = 16.8$ Hz); 6.34 (dd, 1H, $J_1 = 10.3$ Hz, $J_2 = 16.8$ Hz); 7.24−7.41 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 16.3; 18.5; 21.5; 24.4; 24.9; 31.1; 34.2; 42.5; 46.8; 57.4; 72.8; 79.3; 125.2 (2C); 125.9; 127.2; 128.0 (2C); 129.2; 130.8; 139.7; 141.8; 165.4. IR (film): 3015; 1680; 1640; 1600; 780; 750; 730; 690 cm^{-1}. Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 78.33; H, 8.66; N, 3.87.

Synthesis of Amides *epi*-2a and *epi*-2d. A mixture of amide **2a** or **2d** (6.0 mmol) and a chloroform solution of hydrogen chloride (50 mL), obtained by bubbling dry hydrogen chloride though of 50 mL of anhydrous chloroform for 5 s, were agited at room temperature for 20 min. Anhydrous Na_2CO_3 was added, the mixture was filtered, the solvent was eliminated under vacuum, and the residue was purified by flash chromatography on silica gel with hexane/EtOAc 12/1 as eluent for *epi*-**2a** and hexane/EtOAc 10/1 for *epi*-**2d**.

***N*-Acryloyl-2β-(2-*trans*-phenylethenyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (*epi*-2a).** Yield: 38%. Colorless solid. Mp: 92−93 °C (from hexane). $[\alpha]^{25}_D = -29.2$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.83−1.12 (m, 3H); 0.95 (d, 3H, $J = 6.6$ Hz); 1.25−1.52 (m, 2H); 1.37 (s, 3H); 1.67 (s, 3H); 1.65−1.74 (m, 2H); 1.97−2.04 (m, 1H); 3.70 (dt, 1H, $J_1 = 4.4$ Hz, $J_2 = 10.5$ Hz); 5.56 (dd, 1H, $J_1 = 1.7$ Hz, $J_2 = 10.5$ Hz); 6.14−6.22 (m, 3H); 6.56 (dd, 1H, $J_1 = 2.7$ Hz, $J_2 = 16.9$ Hz); 6.55 (dd, 1H, $J_1 = 10.5$ Hz, $J_2 = 16.7$ Hz); 7.24−7.37 (m, 5H). ^{13}C NMR ($CDCl_3$) δ:19.9; 21.9; 24.4; 27.6; 30.9; 34.2; 40.8; 49.9; 57.8; 68.1; 82.6; 126.4 (2C); 126.6; 128.0; 128.4; 128.5 (2C); 131.4; 132.8; 135.6; 167.6. IR (Nujol): 3020; 3070; 1640; 1590; 790; 750; 710; 690 cm^{-1}. Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 77.68; H, 8.77; N, 3.96.

***N*-Acryloyl-2β-[2-*trans*-(2′-nitrophenyl)ethenyl]-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (*epi*-2d).** Yield: 42%. Colorless oil. $[\alpha]^{25}_D = +22.7$ ($c = 0.7$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.91−1.62 (m, 5H); 0.98 (d, 3H, $J = 6.6$ Hz); 1.35 (s, 3H); 1.66 (s, 3H); 1.70−1.78 (m, 2H); 1.97−2.08 (m, 1H); 3.84 (dt, 1H, $J_1 = 4.3$ Hz, $J_2 = 10.6$ Hz); 5.64 (dd, 1H, $J_1 = 1.7$ Hz, $J_2 = 10.5$ Hz); 6.04 (dd, 1H, $J_1 = 3.0$ Hz, $J_2 = 15.9$ Hz); 6.18−6.25 (m, 2H); 6.59 (dd, 1H, $J_1 = 16.7$ Hz, $J_2 = 10.5$ Hz); 7.08 (dd, 1H, $J_1 = 2.0$ Hz, $J_2 = 15.9$ Hz); 7.41−7.67 (m, 3H); 7.99 (dd, 1H, $J_1 = 1.2$ Hz, $J_2 = 8.2$ Hz). ^{13}C NMR ($CDCl_3$) (δ): 19.9; 22.0; 24.5; 27.4; 31.0; 34.3; 40.8; 49.8; 57.9; 68.4; 82.1; 124.7; 127.1; 128.5; 128.6; 128.9; 131.7; 132.1; 133.3; 133.5; 147.6; 167.7. IR (film): 3060; 1680; 1650; 1600; 730; 700 cm^{-1}. MS (*m*/*z*): 384 (M^+, 4); 182 (12); 112 (24); 81 (31); 55 (100). Anal. Calcd for $C_{22}H_{28}N_2O_4$: C, 68.73; H, 7.34; N, 7.29. Found: C, 68.78; H, 7.16; N, 7.12.

General Procedure for Diels−Alder Reactions. A solution of the amide (15 mmol) in the appropriate solvent (50 mL) was refluxed until the reaction was finished (TLC, 3−5 h). The solvent was eliminated under reduced pressure and the residue was chromatographed on silica gel with hexane/EtOAc as eluent. When DMF was used as solvent, the reaction mixture was diluted with 200 mL of Et_2O, washed three times with water and dried over anhydrous $MgSO_4$.

Cycloadduct (3a). Colorless solid. Mp: 192−193 °C (from hexane). $[\alpha]^{25}_D = -177.4$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.74−1.16 (m, 3H); 0.95 (d, 3H, $J = 6.5$ Hz); 1.20 (s, 3H); 1.25 (m, 1H); 1.50 (m, 1H); 1.70−1.78 (m, 2H); 1.77 (s, 3H); 1.91−2.16 (m, 3H); 2.76 (t, 1H, $J = 15.9$ Hz); 2.81 (t, 1H, $J = 15.9$ Hz); 3.18 (dd, 2H, $J_1 = 4.6$ Hz, $J_2 = 15.9$ Hz); 3.42 (dt, 1H, $J_1 = 4.3$ Hz, $J_2 = 10.6$ Hz); 4.71 (d, 1H, $J = 7.4$ Hz); 7.12−7.26 (m, 4H). ^{13}C NMR ($CDCl_3$) δ: 18.5; 22.0; 23.8; 25.9; 29.7; 31.2; 31.8; 34.4; 41.0; 42.4; 43.4; 49.4; 56.8; 76.0; 88.4; 126.1 (2C); 129.8; 130.1; 135.2; 135.3; 173.4. IR (Nujol): 3050; 1690; 750 cm^{-1}. MS (*m*/*z*): 341 ($M^+ + 2$, 25); 340 ($M^+ + 1$, 100). Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 78.01; H, 8.75; N, 3.97.

Cycloadduct (3b). Colorless solid. Mp: 133−134 °C (from hexanes−EtOAc 10−1). $[\alpha]^{25}_D = -168.4$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.75−1.10 (m, 3H); 0.88 (d, 3H, $J = 6.5$ Hz); 1.13 (s, 3H); 1.26 (m, 1H); 1.44 (m, 1H); 1.56−1.72 (m, 2H); 1.69 (s, 3H); 1.86 (m, 1H); 1.93−2.06 (m, 2H); 2.33 (dd, 1H, $J_1 = 12.0$ Hz, $J_2 = 16.6$ Hz); 2.73 (dd, 1H, $J_1 = 12.5$ Hz, $J_2 = 16.2$ Hz); 3.09 (dd, 1H, $J_1 = 4.8$ Hz, $J_2 = 16.2$ Hz); 3.24 (dd, 1H, $J_1 = 4.9$ Hz, $J_2 = 16.6$ Hz); 3.34 (dt, 1H, $J_1 = 4.2$ Hz, $J_2 = 10.6$ Hz); 3.74 (s, 3H); 4.65 (d, 1H, $J = 7.6$ Hz); 6.61 (d, 1H, $J = 8.1$ Hz); 6.72 (d, 1H, $J = 8.1$ Hz); 7.05 (t, 1H, $J = 8.1$ Hz). ^{13}C NMR ($CDCl_3$) δ: 18.5; 22.0; 23.8; 25.9 (2C); 29.9; 31.2; 34.4; 41.0; 42.1; 43.0; 49.4; 55.2; 56.7; 75.9; 88.7; 107.4; 122.1; 124.5; 126.6; 136.8; 157.7; 173.5. IR (Nujol): 3050; 1690; 760; 710; 670 cm^{-1}. MS (*m*/*z*): 371 ($M^+ + 2$, 26); 370 ($M^+ + 1$, 100). Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.59; H, 8.29; N, 3.94.

Cycloadduct (3c). Colorless solid. Mp: 165−166 °C (from hexanes−EtOAc 10−1). $[\alpha]^{25}_D = -131.1$ ($c = 1.3$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.89−1.12 (m, 3H); 0.95 (d, 3H, $J = 6.5$ Hz); 1.19 (s, 3H); 1.31 (m, 1H); 1.48 (m, 1H); 1.72−1.79 (m, 2H);

1.76 (s, 3H); 1.91−2.06 (m, 3H); 2.66 (t, 1H, J = 14.0 Hz); 2.77 (t, 1H, J = 12.4 Hz); 3.07−3.16 (m, 2H); 3.41 (dt, 1H, J_1 = 4.0 Hz, J_2 = 10.5 Hz); 3.75 (s, 3H); 4.69 (d, 1H, J = 7.4 Hz); 6.68 (s, 1H); 6.69 (d, 1H, J = 7.9 Hz); 7.01 (d, 1H, J = 7.9 Hz). ^{13}C NMR ($CDCl_3$) δ: 18.3; 21.9; 23.7; 25.7; 29.9; 30.8; 31.0; 34.2; 40.8; 42.5; 43.3; 49.3; 55.0; 56.6; 75.7; 88.2; 112.4; 114.2; 127.1; 130.4; 136.3; 157.6; 173.2. IR (Nujol): 3050; 1680; 790; 760 cm^{-1}. MS (m/z): 369 (M^+, 10); 159 (59); 81 (48); 58 (100); 55 (75); 41 (89). Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.58; H, 8.62; N, 3.62.

Cycloadduct (3d). Colorless solid. Mp: 194−195 °C (from hexanes−EtOAc 8−1). $[\alpha]^{25}_D$ = −496.9 (c = 1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.78−1.10 (m, 3H); 0.95 (d, 3H, J = 6.5 Hz); 1.22 (s, 3H); 1.30 (m, 1H); 1.45 (m, 1H); 1.60−1.78 (m, 2H); 1.77 (s, 3H); 1.87 (m, 1H); 2.01 (m, 1H); 2.15 (dt, 1H, J_1 = 5.1 Hz, J_2 = 12.5 Hz); 2.90 (dd, 1H, J_1 = 12.5 Hz, J_2 = 16.5 Hz); 3.01 (dd, 1H, J_1 = 12.5 Hz, J_2 = 17.0 Hz); 3.27 (dd, 1H, J_1 = 5.1 Hz, J_2 = 16.5 Hz); 3.33 (dd, 1H, J_1 = 5.0 Hz, J_2 = 17.0 Hz); 3.44 (dt, 1H, J_1 = 4.2 Hz, J_2 = 10.6 Hz); 4.79 (d, 1H, J = 7.5 Hz); 7.30 (t, 1H, J = 7.6 Hz); 7.40 (d, 1H, J = 7.6 Hz); 7.73 (d, 1H, J = 7.6 Hz). ^{13}C NMR ($CDCl_3$) (δ): 18.5; 21.9; 23.7; 25.8; 29.1; 30.3; 31.1; 34.3; 40.8; 41.7; 42.2; 49.3; 57.0; 75.9; 88.0; 122.5; 126.7; 130.1; 134.8; 138.4; 150.6; 172.3. IR (Nujol): 3050; 1690; 800; 780; 770; 740 cm^{-1}. MS (m/z): 386 (M^+ + 2, 25); 385 (M^+ + 1, 100). Anal. Calcd for $C_{22}H_{28}N_2O_4$: C, 68.73; H, 7.34; N, 7.29. Found: C, 68.90; H, 7.46; N, 7.11.

Cycoadduct (3e). Colorless solid. Mp: 149−150 °C (from hexanes−EtOAc 10−1). $[\alpha]^{25}_D$ = −146.4 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.86−1.12 (m, 3H); 0.92 (s, 3H); 0.95 (d, 3H, J = 6.5 Hz); 1.91 (s, 3H); 1.30−1.36 (m, 1H); 1.40−1.62 (m, 1H); 1.72−1.80 (m, 2H); 1.79 (s, 3H); 2.00−2.09 (m, 2H); 2.77 (m, 1H); 2.79 (d, 1H, J = 16.0 Hz); 2.94 (d, 1H, J = 16.0 Hz); 3.07 (dd, 1H, J_1 = 5.0 Hz, J_2 = 15.9 Hz); 3.42 (dt, 1H, J_1 = 4.1 Hz, J_2 = 10.6 Hz); 4.75 (d, 1H, J = 8.2 Hz); 7.13−7.26 (m, 4H). ^{13}C NMR ($CDCl_3$) δ: 15.3; 18.4; 21.9; 23.9; 25.9; 26.6; 31.2; 34.4; 37.9; 41.0; 41.9; 44.5; 49.5; 56.6; 76.0; 86.9; 125.8; 126.2; 129.7; 130.8; 134.6; 134.9; 177.4. IR (Nujol): 3050; 1685; 775; 750 cm^{-1}. MS (m/z): 355 (M^+ + 2, 25); 354 (M^+ + 1, 100). Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 78.34; H, 8.72; N, 4.17.

Cycloadduct (3g). Colorless solid. Mp: 177−178 °C (from hexanes−EtOAc 10−1). $[\alpha]^{25}_D$ = −263.7 (c = 1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.86−1.01 (m, 2H); 0.98 (s, 3H); 0.99 (d, 3H, J = 6.8 Hz); 1.13 (q, 1H, J = 11.8 Hz); 1.28 (m, 1H); 1.33−1.62 (m, 1H); 1.63−1.80 (m, 2H); 1.71 (s, 3H); 2.14 (m, 1H); 2.27−2.37 (m,2H); 2.88 (m, 1H); 3.23−3.33 (m, 2H); 4.22 (d, 1H, J = 7.6 Hz); 4.67 d, 1H, J = 4.1 Hz); 6.92−7.31 (m, 9H). ^{13}C NMR ($CDCl_3$) δ: 18.0; 22.0; 23.7; 25.8; 29.8; 31.1; 34.3; 36.5; 41.0; 44.3; 46.5; 49.4; 56.5; 75.7; 85.4; 126.4 (2C); 126.6; 128.1 (2C); 129.7; 130.0 (2C); 131.1; 136.0; 137.7; 141.8; 172.5. IR (Nujol): 3050; 1700; 1590; 750; 700 cm^{-1}. MS (m/z): 417 (M^+ + 2, 30); 416 (M^+ + 1, 100). Anal. Calcd for $C_{28}H_{33}NO_2$: C, 80.93; H, 8.00; N, 3.37. Found: C, 81.14; H, 8.18; N, 3.22.

Cycloadduct (*epi*-3a). Colorless solid. Mp: 205−206 °C (from hexanes−EtOAc 8−1). $[\alpha]^{25}_D$ = +197.2 (c = 1.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.89−1.41 (m, 3H); 0.97 (d, 3H, J = 6.5 Hz); 1.43 (s, 3H); 1.53 (s, 3H); 1.49 (m, 1H); 1.65−1.83 (m, 3H); 1.87 (m, 1H); 2.00 (m, 1H); 2.22 (dt, 1H, J_1 = 5.3 Hz, J_2 = 12.5 Hz); 2.75 (dd, 1H, J_1 = 12.5 Hz, J_2 = 15.6 Hz); 2.80 (dd, 1H, J_1 = 12.5 Hz, J_2 = 15.6 Hz); 3.12 (dd, 1H, J_1 = 5.4 Hz, J_2 = 15.6 Hz); 3.15 (dd, 1H, J_1 = 5.4 Hz, J_2 = 15.6 Hz); 3.75 (dt, 1H, J_1 = 4.0 Hz, J_2 = 11.2 Hz); 5.14 (d, 1H, J = 6.7 Hz); 7.16−7.80 (m, 4H). ^{13}C NMR ($CDCl_3$) δ: 19.2; 21.9; 23.0; 24.3; 29.7; 31.3; 31.8; 34.3; 42.0; 42.9; 45.0; 47.0; 55.4; 74.3; 83.3; 126.0 (2C); 129.7; 130.0; 135.1 (2C); 172.9. IR (Nujol): 3040, 1680, 760, 740 cm^{-1}. Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 77.96; H, 8.80; N, 4.02.

Cycloadduct (*epi*-3d). Colorless solid. Mp: 188−189 °C (from hexanes−EtOAc 8−1). $[\alpha]^{25}_D$ = +470.3 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.78−1.28 (m, 3H); 0.97 (d, 3H, J = 6.5 Hz); 1.36−1.61 (m, 1H); 1.43 (s, 3H); 1.54 (s, 3H); 1.68−1.81 (m, 4H); 1.82−2.04 (m, 1H); 2.26 (dt, 1H, J_1 = 5.1 Hz, J_2 = 12.6 Hz); 2.89 (dd, 1H, J_1 = 12.6 Hz, J_2 = 16.3 Hz); 2.99 (dd, 1H, J_1 = 12.5 Hz, J_2 = 17.0 Hz); 3.21 (dd, 1H, J_1 = 5.1 Hz, J_2 = 16.3 Hz); 3.27 (dd, 1H, J_1 = 4.8 Hz, J_2 = 17.0 Hz); 3.75 (dt, 1H, J_1 = 3.9 Hz, J_2 = 11.2 Hz); 5.23 (d, 1H, J = 6.6 Hz); 7.29 (t, 1H, J = 7.4 Hz); 7.42 (d, 1H, J = 7.4 Hz); 7.70 (d, 1H, J = 7.4 Hz). ^{13}C NMR ($CDCl_3$) δ: 19.1; 21.8; 22.9; 24.2; 29.0; 30.3; 31.2; 34.1; 41.6; 41.8; 44.2; 46.9; 55.6; 74.3; 83.0; 122.4; 126.6; 130.0; 134.6; 138.3; 150.4; 171.9. IR (Nujol): 3050; 1690; 740 cm^{-1}. MS (m/z): 384 (M^+, 8); 128 (61); 81 (61); 55 (82); 41 (100). Anal. Calcd for $C_{22}H_{28}N_2O_4$: C, 68.73; H, 7.34; N, 7.29. Found: C, 68.90; H, 7.51; N, 7.12.

Cycloadduct (6). Colorless oil. $[\alpha]^{25}_D$ = −98.1 (c = 1.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.79 (d, 3H, J = 7.5 Hz); 0.90−0.94 (m, 2H); 0.92 (d, 3H, J = 6.3 Hz); 1.07 (q, 1H, J = 12.0 Hz); 1.20 (s, 3H); 1.33 (m, 1H); 1.48 (m, 1H); 1.65−1.80 (m, 2H); 1.77 (s, 3H); 2.00 (m, 1H); 2.56 (m, 1H); 3.39 (m, 1H); 3.45 (dt, 1H, J_1 = 4.0 Hz, J_2 = 10.5 Hz); 5.12 (d, 1H, J = 7.1 Hz); 5.19 (s, 1H); 5.49 (s, 1H); 7.11−7.36 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 11.9; 17.7; 21.5; 23.5; 25.2; 30.7; 33.9; 38.8; 40.6; 45.4; 49.2; 56.2; 75.7; 85.7; 113.3; 125.4 (2C); 127.2; 127.9 (2C); 140.5; 143.3; 174.4. IR (film): 3050; 2930; 1730; 1680; 1640; 780; 720; 700 cm^{-1}. Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 78.33; H, 8.99; N, 4.08.

Synthesis of Amino Alcohols 7 and 9a−g. General Method. To a suspension of $LiAlH_4$ (0.57 g, 15 mmol) in anhydrous THF (40 mL) cooled to −10 °C was added, in portions, dry $AlCl_3$ (0.67 g, 5 mmol). The mixture was stirred for 10 min, and a solution of the corresponding adduct (3 mmol) in dry THF (20 mL) was slowly added. The reaction mixture was stirred fo 8 min at −10 °C and quenched by addition of H_2O (4 mL). The resulting mixture was filtered, the solid was washed with EtOAc, and the organic layer was dried ($MgSO_4$). The solvent was eliminated under reduced pressure, and the residue was chromatographed on silica gel using hexane/EtOAc 3/1 as eluent.

(3a*R*,9a*R*)-*N*-(8-Mentholyl)-3a,4,9,9a-tetrahydrobenz[*f*]-isoindoline (9a). Yield: 80%. Colorless solid. Mp: 148−149 °C (from hexane). $[\alpha]^{25}_D$ = −54.6 (c = 1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 333 K) δ: 0.85−1.13 (m, 3H); 0.91 (d, 3H, J = 6.5 Hz); 0.97 (s, 3H); 1.19 (s, 3H); 1.49−1.36 (m, 2H); 1.57−1.70 (m, 2H); 1.73−1.90 (m, 2H); 1.93 (m, 1H); 2.52−2.64 (m, 4H); 2.91−3.00 (m, 2H); 3.13−3.20 (m, 2H); 3.65 (dt, 1H, J_1 = 4.0 Hz, J_2 = 10.4 Hz); 7.07 (s, 4H); 8.70 (broad s, 1H). ^{13}C NMR ($CDCl_3$, 333 K) δ: 16.5; 21.3; 22.0; 25.7; 31.0; 33.6 (2C); 35.2; 41.2 (2C); 44.3; 49.4; 51.3 (2C); 59.6; 72.9; 125.8 (2C); 129.5 (2C); 136.0 (2C). IR (Nujol): 3250 (broad); 750 cm^{-1}. MS (m/z): 329 (M^+ + 2, 26); 328 (M^+ + 1, 100); 326 (20); 214 (26).

(3a*R*,9a*R*)-*N*-(8-Mentholyl)-5-methoxy-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline (9b). Yield: 88%. Colorless oil. $[\alpha]^{25}_D$ = −61.3 (c = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 333 K) δ: 0.83−1.10 (m, 2H); 0.91 (d, 3H, J = 6.5 Hz); 0.94 (s, 3H); 1.11 (s, 3H); 1.26−1.50 (m, 2H); 1.55−1.90 (m, 4H); 1.94 (m, 1H); 2.21 (m, 1H); 2.48−2.58 (m, 3H); 2.87 (m, 1H); 3.03−3.17 (m, 3H); 3.63 (dt, 1H, J_1 = 4.0 Hz, J_2 = 10.4 Hz); 3.76 (s, 3H); 6.62 (d, 1H, J = 8.0 Hz); 6.67 (d, 1H, J = 7.7 Hz); 6.72 (dd, 1H J_1 = 7.7 Hz, J_2 = 8.0 Hz); 9.50 (broad s, 1H). ^{13}C NMR ($CDCl_3$, 333 K) δ: 16.3; 21.0; 21.8; 25.5; 29.7; 30.8; 33.6; 35.0; 40.4; 40.7; 44.2; 49.2; 51.0; 51.3; 54.9; 59.4; 72.6; 107.2; 121.5; 125.0; 125.9; 137.2; 157.4. IR (film): 3400 (broad); 1570; 700; 680; 650 cm^{-1}. MS (m/z): 357 (M^+, 0.5); 244 (100); 55 (16); 43 (40); 41 (32).

(3a*R*,9a*R*)-*N*-(8-Mentholyl)-6-methoxy-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline (9c). Yield: 94%. Colorless solid. Mp: 110−111 °C (from hexanes−EtOAc 15/1). $[\alpha]^{25}_D$ = −55.0 (c = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 333 K) δ: 0.83−1.08 (m, 3H); 0.91 (d, 3H, J = 6.5 Hz); 0.96 (s, 3H); 1.18 (s, 3H); 1.40−1.48 (m, 2H); 1.55−1.70 (m, 2H); 1.74−1.93 (m, 2H); 1.95 (m, 1H); 2.44−2.60 (m, 4H); 2.85−2.92 (m, 2H); 3.12−3.16 (m, 2H); 3.64 (dt, 1H, J_1 = 4.0 Hz, J_2 = 10.2 Hz); 3.74 (s, 3H); 6.61 (d, 1H, J = 2.5 Hz); 6.66 (dd, 1H, J_1 = 2.5 Hz, J_2 = 8.4 Hz); 6.97 (d, 1H J = 8.4 Hz); 8.55 (broad s, 1H). ^{13}C NMR ($CDCl_3$, 333 K) δ: 16.6; 21.3; 22.0; 25.8; 31.1; 32.9; 33.9; 35.3; 41.2; 41.5; 44.5; 49.5; 51.3 (2C); 55.2; 59.7; 72.9; 112.2; 114.4; 128.3; 130.2; 137.3; 157.9. IR (Nujol): 3100 (broad); 1610 cm^{-1}. MS (m/z): 357 (M^+, 0.5); 244 (47); 110 (43); 70 (40); 55 (48); 43 (60); 41 (100).

(3a*R*,9a*R*)-*N*-(8-Mentholyl)-5-nitro-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline (9d). Yield: 83%. Colorless solid. Mp: 68−69 °C (from hexanes−EtOAc 8/1). $[\alpha]^{25}_D$ = −342.3 (c

= 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 333 K) δ: 0.85−1.07 (m, 3H); 0.92 (d, 3H, J = 6.5 Hz); 0.98 (s, 3H); 1.19 (s, 3H); 1.39−1.49 (m, 2H); 1.57−1.85 (m, 4H); 1.92 (m, 1H); 2.61−2.83 (m, 4H); 3.04−3.22 (m, 4H); 3.64 (dt, 1H, J_1 = 4.0 Hz, J_2 = 10.4 Hz); 7.22 (dd, 1H, J_1 = 7.5 Hz, J_2 = 7.8 Hz); 7.32 (d, 1H J = 7.5 Hz); 7.64 (d, 1H, J = 7.8 Hz); 8.45 (broad s, 1H). ^{13}C NMR ($CDCl_3$, 333 K) δ: 16.6; 21.3; 22.0; 25.7; 30.3; 31.1; 34.2; 35.2; 40.0; 40.5; 44.4; 49.5; 51.0; 51.3; 59.7; 72.9; 122.1; 126.3; 130.8; 134.0; 139.3; 150.8. IR (Nujol): 3100 (broad); 790; 730 cm^{-1}. MS (m/z): 372 (M^+, 1); 259 (100); 115 (23); 70 (62); 41 (89).

(3a*R*,9a*R*)-*N*-(8-Mentholyl)-3a-methyl-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline (9e). Yield: 91%. Colorless oil. $[\alpha]^{25}_D$ = −65.0 (c = 1.4, $CHCl_3$). ^1H NMR ($CDCl_3$, 333 K) δ: 0.83−1.07 (m, 3H); 0.88 (s, 3H); 0.92 (d, 3H, J = 6.5 Hz); 0.96 (s, 3H); 1.16 (s, 3H); 1.38−1.48 (m, 2H); 1.57−1.70 (m, 2H); 1.83−1.95 (m, 2H); 2.48−2.85 (m, 7H); 3.04 (dd, 1H, J_1 = 8.4 Hz, J_2 = 9.7 Hz); 3.64 (dt, 1H, J_1 = 4.0 Hz, J_2 = 10.3 Hz); 7.09 (broad s, 4H); 8.55 (broad s, 1H). ^{13}C NMR ($CDCl_3$, 333 K) δ: 16.7; 17.1; 21.3; 22.0; 25.6; 28.9; 31.0; 35.2; 38.5; 41.9; 43.1; 44.4; 48.3; 49.4; 59.1; 59.4; 72.8; 125.6; 125.9; 129.4; 130.1; 135.4; 135.7. IR (film): 3100 (broad); 730; 720 cm^{-1}. MS (m/z): 341 (M^+, 1); 228 (100); 104 (34); 91 (61); 41 (90).

(3a*S*,4*R*,9a*R*)-*N*-(8-Mentholyl)-4-phenyl-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline (9g). Yield: 93%. Colorless solid. Mp: 146−147 °C (from hexane). $[\alpha]^{25}_D$ = −145.4 (c = 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$, 333 K) δ: 0.67 (s, 3H); 0.79−1.01 (m, 3H); 0.89 (d, 3H, J = 6.5 Hz); 1.05 (s, 3H); 1.26−1.45 (m, 2H); 1.51 (m, 1H); 1.66 (m, 1H); 1.83−2.10 (m, 3H); 2.15 (m, 1H); 2.59−2.69 (m, 2H); 2.95 (dd, 1H, J_1 = 6.1 Hz, J_2 = 8.9 Hz); 3.01−3.11 (m, 2H); 3.57 (dt, 1H, J_1 = 4.0 Hz, J_2 = 10.3 Hz); 4.35 (d, 1H, J = 5.8 Hz); 6.84−6.88 (m, 2H); 6.93−6.95 (m, 1H); 7.02−7.24 (m, 6H); 8.45 (broad s, 1H). ^{13}C NMR ($CDCl_3$, 333 K) δ: 16.5; 21.2; 22.0; 25.8; 31.1; 33.6; 34.4; 35.4; 44.5 (2C); 46.5; 48.7; 49.4; 51.0; 59.8; 72.8; 126.2; 126.3 (2C); 127.8 (2C); 129.3; 129.9 (2C); 131.3; 136.8; 139.0; 142.8. IR (Nujol): 3100 (broad); 760; 740; 730; 700 cm^{-1}. MS (m/z): 403 (M^+, 1); 290 (100); 91 (82); 41 (74).

(3a*S*, 9a*S*)-*N*-(8-Mentholyl)-3a,4,9,9a-tetrahydrobenz-[*f*]isoindoline (*epi*-9a). Yield: 87%. Colorless solid. Mp: 153−154 °C (from hexane). $[\alpha]^{25}_D$ = +53.9 (c = 1.3, $CHCl_3$). ^1H NMR ($CDCl_3$, 333 K) δ: 0.84−1.08 (m, 3H); 0.91 (d, 3H, J = 6.5 Hz); 0.96 (s, 3H); 1.19 (s, 3H); 1.43 (m, 1H); 1.52−1.63 (m, 2H); 1.67 (m, 1H); 1.74−1.91 (m, 2H); 1.93 (m, 1H); 2.48−2.63 (m, 4H); 2.94 (dd, 2H, J_1 = 2.6 Hz, J_2 = 16.8 Hz); 3.26 (dd, 2H, J_1 = 7.1 Hz, J_2 = 7.9 Hz); 3.64 (dt, 1H, J_1 = 4.0 Hz, J_2 = 10.2 Hz); 7.06 (s, 4H); 8.20 (broad s, 1H).^{13}C NMR ($CDCl_3$, 333 K) δ: 18.3; 21.5; 22.0; 26.0; 31.2; 33.8 (2C); 35.3; 41.3 (2C); 44.4; 48.9; 50.7 (2C); 59.3; 73.0; 125.8 (2C); 129.5 (2C); 136.3 (2C). IR (Nujol): 3150 (broad); 770 cm^{-1}. MS (m/z): 329 (M^+ + 2, 24); 328 (M^+ + 1, 100); 326 (19); 214 (35).

(3a*S*,9a*S*)-*N*-(8-Mentholyl)-5-nitro-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline (*epi*-9d). Yield: 81%. Colorless oil. $[\alpha]^{25}_D$ = +256.5 (c = 0.9, $CHCl_3$). ^1H NMR ($CDCl_3$, 333 K) δ: 0.87−1.15 (m, 3H); 0.91 (d, 3H, J = 6.5 Hz); 0.98 (s, 3H); 1.20 (s, 3H); 1.42 (m, 1H); 1.52−1.95 (m, 6H); 2.48−2.82 (m, 4H); 3.02−3.16 (m, 2H); 3.26−3.33 (m, 2H); 3.63 (dt, 1H, J_1 = 4.0 Hz, J_2 = 10.3 Hz); 7.21 (dd, 1H, J_1 = 7.6 Hz, J_2 = 7.8 Hz); 7.31 (d, 1H, J = 7.6 Hz); 7.63 (d 1H, J = 7.8 Hz); 9.31 (broad s, 1H). ^{13}C NMR ($CDCl_3$, 333 K) δ: 18.1; 21.3; 21.9; 25.8; 30.4; 31.0; 34.2; 35.1; 39.9; 40.5; 44.2; 48.8; 50.4; 50.5; 59.3; 72.9; 121.9; 126.1; 130.8; 133.9; 139.3; 150.7. IR (film): 3110 (broad); 820; 790; 730 cm^{-1}. MS (m/z): 372 (M^+, 1); 259 (75); 55 (64); 41 (100).

***N*-(8-Mentholyl)-3-methyl-4-(1-phenylethenyl)pyrrolidine (7).** Yield: 82%. Colorless oil. $[\alpha]^{25}_D$ = +15.4 (c = 0.9, $CHCl_3$). ^1H NMR ($CDCl_3$, 333 K) δ: 0.68 (d, 3H, J = 7.0 Hz); 0.84−1.09 (m, 3H); 0.91 (d, 3H, J = 6.5 Hz); 0.98 (s, 3H); 1.19 (s, 3H); 1.38−1.53 (m, 2H); 1.55−1.69 (m, 2H); 1.95 (m, 1H); 2.25 (dq, 1H, J_1 = 2.6 Hz, J_2 = 7.0 Hz); 2.43 (m, 1H); 2.97 (m, 1H); 3.05 (dd, 1H, J_1 = 7.1 Hz, J_2 = 9.0 Hz); 3.20 (m, 1H); 3.26 (m, 1H); 3.64 (dt, 1H, J_1 = 4.0 Hz, J_2 = 10.2 Hz); 5.00 (s, 1H); 5.33 (s, 1H); 7.18−7.35 (m, 5H); 8.45 (broad s, 1H). ^{13}C NMR ($CDCl_3$, 333 K) δ: 15.2; 16.6; 21.5; 21.9; 25.6; 30.9; 33.1; 35.1; 44.3; 45.3; 47.0; 48.7; 53.3; 59.0; 72.7; 112.8; 126.0 (2C); 127.1; 128.1 (2C); 142.2; 147.0. IR (film): 3100 (broad); 1620; 780; 710; 700 cm^{-1}.

Elimination of the Menthol Appendage. General Method. A solution of amino derivatives **7** and **9a**−**g** (1.0 mmol) and PCC (1.3 g, 6 mmol) in CH_2Cl_2 (40 mL) and 4 Å molecular sieves (1 g) was stirred at room temperature until the oxidation was finished (TCL, 6−8 h). The solvent was eliminated under reduced pressure, the residue was dissolved in 15% aqueous solution of NaOH (25 mL), and the resulting solution was extracted with EtOAc. The organic phase was washed with brine and dried over anhydrous magnesium sulfate. The solvents were eliminated under vacuum, and the residue was taken up in a 2.5 M solution (16 mL) of KOH in THF/MeOH/H_2O (2/1/1), and the solution was stirred at room temperature for 5−6 h. After elimination of the solvents under reduced pressure, the residue was dissolved in 50 mL of CH_2Cl_2 and washed with H_2O. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was eliminated under vacuum to give an oily residue which was purified by flash chromatography on silica gel using a mixture of $CHCl_3$/EtOH 8/1 as eluent. The benzoisoindolines **10a**−**h**, *ent*-**10a**, and *end*-**10d** were characterized as hydrochorides and the pyrrolidine **8** as the tosylate.

(3a*R*,9a*R*)-3a,4,9,9a-Tetrahydrobenz[*f*]isoindoline Hydrochoride (10a). Yield: 68%. Colorless solid. Mp: 208−209 °C (from EtOH−Et_2O). $[\alpha]^{25}_D$ = −60.1 (c = 0.9, MeOH). ^1H NMR (DMSO) δ: 2.29 (m, 2H); 2.94 (m, 2H); 3.22 (m, 2H); 3.37 (m, 2H); 3.91 (m, 2H); 7.48 (s, 4H); 9.50 (broad s, 2H). ^{13}C NMR (DMSO) δ: 32.6 (2C); 40.4 (2C); 49.7 (2C); 126.8 (2C); 130.1 (2C); 135.5 (2C). IR (Nujol): 3400 (broad); 2700; 2400; 760 cm^{-1}. Anal. Calcd for $C_{12}H_{16}ClN$: C, 68.73; H, 7.69; N, 6.68. Found: C, 68.51; H, 7.87; N, 6.52.

(3a*R*,9a*R*)-5-Methoxy-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline hydrochloride (10b). Yield: 80%. Colorless solid. Mp: 294−295 °C (from EtOH−Et_2O). $[\alpha]^{25}_D$ = −90.7 (c = 0.9, MeOH). ^1H NMR (DMSO) δ: 2.17 (m, 2H); 2.51 (m, 1H); 2.80−2.91 (m, 1H); 3.12−3.24 (m, 2H); 3.25−3.40 (m, 2H); 3.86 (m, 2H); 4.04 (s, 3H); 7.03 (d, 1H, J = 7.8 Hz); 7.07 (d, 1H, J = 7.8 Hz); 7.42 (t, 1H, J = 7.8 Hz). ^{13}C NMR (DMSO) δ: 26.6; 32.4; 39.9; 40.1; 49.7; 49.9; 55.8; 108.4; 122.1; 123.9; 127.4; 136.8; 157.6. IR (Nujol): 2680; 1580; 760; 700; 690 cm^{-1}. Anal. Calcd for $C_{13}H_{18}ClNO$: C, 65.13; H, 7.57; N, 5.84. Found: C, 64.97; H, 7.76; N, 5.65.

(3a*R*,9a*R*)-6-Methoxy-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline Hydrochloride (10c). Yield: 78%. Colorless solid. Mp: 243−244 °C (from EtOH−Et_2O). $[\alpha]^{25}_D$ = −73.6 (c = 0.9, MeOH). ^1H NMR (DMSO) δ: 2.17 (m, 2H); 2.64−2.85 (m, 2H); 3.08−3.26 (m, 4H); 3.81 (m, 2H); 3.95 (s, 3H); 6.93 (d, 1H, J = 2.6 Hz); 6.97 (dd, 1H, J_1 = 2.6 Hz, J_2 = 8.4 Hz); 7.28 (d, 1H, J = 8.4 Hz); 9.43 (broad s, 2H). ^{13}C NMR (DMSO) δ: 31.7; 32.6; 40.7; 41.0; 49.9 (2C); 55.8; 113.2; 114.7; 127.6; 131.1; 136.9; 158.2. IR (Nujol): 3310 (broad); 2700; 2460; 1600; 820; 730 cm^{-1}. Anal. Calcd for $C_{13}H_{18}ClNO$: C, 65.13; H, 7.57; N, 5.84. Found: C, 64.91; H, 7.79; N, 5.70.

(3a*R*,9a*R*)-5-Nitro-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline Hydrochloride (10d). Yield: 62%. Yellow solid. Mp: 325−326 °C (from EtOH−Et_2O). $[\alpha]^{25}_D$ = −447.1 (c = 0.7, MeOH). ^1H NMR (DMSO) δ: 2.22 (m, 2H); 2.85−3.05 (m, 2H); 3.17−3.24 (m, 2H); 3.30−3.46 (m, 2H); 3.86 (m, 2H); 7.65 (t, 1H, J = 7.8 Hz); 7.75 (d, 1H, J = 7.8 Hz); 7.97 (d, 1H, J = 7.8 Hz); 9.51 (broad s, 2H). ^{13}C NMR (DMSO) δ: 29.1; 32.5; 39.1; 39.7; 49.6 (2C); 122.7; 127.6; 129.6; 135.1; 139.0; 150.5. IR (Nujol): 3350; 2700; 2420; 1490; 820; 800; 790; 760; 730 cm^{-1}. Anal. Calcd for $C_{12}H_{15}ClN_2O_2$: C, 56.58; H, 5.94; N, 11.00. Found: C, 56.39; H, 6.10; N, 10.89.

(3a*R*,9a*R*)-3a-Methyl-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline Hydrochloride (10e). Yield: 76%. Colorless solid. Mp: 286−287 °C (from EtOH−Et_2O). $[\alpha]^{25}_D$ = −80.8 (c = 1.1, MeOH). ^1H NMR (DMSO) δ: 1.15 (s, 3H); 2.43 (m, 1H); 2.87 (m, 1H); 3.01 (d, 1H, J = 16.1 Hz); 3.19 (d, 1H, J = 16.1 Hz); 3.20−3.36 (m, 3H); 3.61 (d, 1H, J = 10.9 Hz); 3.81 (dd, 1H, J_1 = 7.9 Hz, J_2 = 10.9 Hz); 7.47 (s, 4H); 9.75 (broad s, 2H). ^{13}C NMR (DMSO) δ: 16.2; 27.9; 38.7; 40.5; 42.4; 47.3; 56.6; 126.6; 126.8; 130.1; 130.7; 134.6; 135.0. IR (Nujol): 2700; 2410; 1590;

750 cm^{-1}. Anal. Calcd for $C_{13}H_{18}ClN$: C, 69.79; H, 8.11; N, 6.26. Found: C, 69.61; H, 8.20; N, 6.14.

(3a*S*,4*R*,9a*R*)-4-Phenyl-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline Hydrochloride (10g). Yield: 80%. Colorless solid. Mp: 273−275 °C (from EtOH−Et_2O). $[\alpha]^{25}_D = -183.9$ ($c = 0.9$, MeOH). ^{1}H NMR ($CDCl_3$) δ: 2.18−2.36 (m, 2H); 2.41 (m, 1H); 2.72 (dd, 1H, $J_1 = 11.4$ Hz, $J_2 = 16.2$ Hz); 2.98 (m, 1H); 3.22 (dd, 1H, $J_1 = 5.2$ Hz, $J_2 = 16.2$ Hz); 3.50−3.60 (m, 2H); 4.45 (d, 1H, $J = 5.8$ Hz); 6.81−6.92 (m, 2H); 7.96 (d, 1H, $J = 7.5$ Hz); 7.07−7.28 (m, 6H); 9.44 (broad s, 1H); 9.72 (broad s, 1H). ^{13}C NMR ($CDCl_3$) δ: 33.0; 33.2; 44.0; 45.0; 47.6; 48.8; 126.7; 126.8; 127.1; 128.4 (2C); 129.1; 129.7 (2C); 131.1; 134.8; 137.1; 140.5. IR (Nujol): 2690; 1570; 750; 740; 730; 690 cm^{-1}. Anal. Calcd for $C_{18}H_{20}ClN$: C, 75.64; H, 7.05; N, 4.90. Found: C, 75.47; H, 7.22; N, 4.73.

(3a*S*,9a*S*)-3a,4,9,9a-Tetrahydrobenz[*f*]isoindoline Hydrochoride (*ent*-10a). Yield: 72%. Colorless solid. Mp: 211−212 °C (from EtOH−Et_2O). $[\alpha]^{25}_D = -60.6$ ($c = 0.7$, MeOH). ^{1}H NMR, ^{13}C NMR, and IR data are coincident with those reported for **10a**.

(3a*S*,9a*S*)-5-Nitro-3a,4,9,9a-tetrahydrobenz[*f*]isoindoline Hydrochloride (*ent*-10d). Yield: 68%. Yellow solid. Mp: 320−322 °C (from EtOH−Et_2O). $[\alpha]^{25}_D = +425.2$ ($c = 0.8$, MeOH). ^{1}H NMR, ^{13}C NMR, and IR data are coincident with those reported for **10d**.

(3*S*,4*S*)-*N*-Tosyl-3-methyl-4-(1-phenylethenyl)pyrrolidine (8). Yield: 82%. Colorless oil. $[\alpha]^{25}_D = +44.2$ ($c = 2.9$, MeOH). ^{1}H NMR ($CDCl_3$) δ: 0.41 (d, 3H, $J = 7.0$ Hz), 2.16 (m, 1H); 2.41 (s, 3H); 3.11 (dd, 1H, $J_1 = 2.1$ Hz, $J_2 = 10.0$ Hz); 3.28 (m, 1H); 3.41 (dd, 1H, $J_1 = 9.3$ Hz, $J_2 = 19.1$ Hz); 3.43 (dd, 1H, $J_1 = 10.0$ Hz, $J_2 = 16.2$ Hz); 3.63 (dd, 1H, $J_1 = 7.0$ Hz, $J_2 = 9.3$ Hz); 4.87 (d, 1H, $J = 1.1$ Hz); 5.27 (d, 1H, $J = 1.1$ Hz); 7.20−7.30 (m, 5H); 7.33 (d, 2H, $J = 8.2$ Hz); 7.77 (d, 2H, $J = 8.2$ Hz). ^{13}C NMR ($CDCl_3$) δ: 13.3; 21.2; 34.2; 45.2; 48.5; 54.6; 113.6; 125.9 (2C); 127.1 (2C); 127.3; 128.1 (2C); 129.4 (2C); 133.7; 141.0; 143.1; 145.4. Anal. Calcd for $C_{20}H_{23}NO_2S$: C, 70.35; H, 6.79; N, 4.10. Found: C, 70.18; H, 6.95; N, 4.26.

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Supporting Information Available: Synthesis and spectroscopic data for *trans*-β-methyl cinnamaldehyde. Physical and spectroscopic data for minor compounds **4a**,**b**,**d**,**e**, *epi*-**4d**, and **5**. X-ray structures for compounds **3a**,**g**, *epi*-**3a**, and **5**. COSY and NOESY experiments for compounds **3b**−**d**, *epi*-**3d**, and **4b**,**d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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